心脏解剖的評估中標準胃腸超聲內鏡的應用

The Use of Standard Gastrointestinal Endoscopic Ultrasound to Assess Cardiac Anatomy

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在這項在一個學術醫療中心進行的前瞻性觀察研究中，我們評估了在基礎的經食管超聲心動圖（TEE）檢查中使用內鏡超聲檢查（EUS）技術來確定評估心臟結構的可行性。當在內鏡中心發生因低血容量、心室功能低下、主動脈夾層、心包積液或主動脈瓣狹窄引起的血流動力學突發事件，這項技術可能存在潛在的益處。在登記的 20 例患者中，18 例在標準的臨床適應征下使用線性超聲內鏡行內鏡超聲檢查（EUS）和由具有 TEE 執照的心臟麻醉醫師的指導下進行心臟評估。20 例病患中有 8 例可以使用線性超聲內鏡獲得 1999 版美國超聲心動圖協會和心血管麻醉醫師協會 TEE 指南所認可的心血管結構的標準影像。以下這些心臟瓣膜結構可以完成視覺化：主動脈瓣（100%）、二尖瓣（100%）、三尖瓣（33%）和肺動脈瓣（11%）。左心室收縮功能和右心室收縮功能分別可以在 89%和 67%的病患中進行評估。其他結構諸如升、降主動脈、心包、左心耳和房間隔都可以在 100%的病患中予以識別。依賴多普勒技術的功能不能被評估。鑒於 EUS 的圖像不能與 TEE 的圖像在這些病患中進行直接的比較，我們不能明確地對這些評估的品質進行評論，在將來的研究中需要進行一個正式的比較。基於這項研究，EUS 技術可以持續評估二尖瓣、主動脈瓣、主動脈、心包和左心室功能。鑒於其局限性，EUS 技術儘管不是一個正式超聲心動圖檢查的替代品，仍可以作為一個有用的早期診斷工具

（俞啟蒙 譯 薛張綱 校）

In this prospective observational study, conducted at an academic medical center, we evaluated the feasibility of performing a basic transesophageal echocardiography (TEE) examination using endoscopic ultrasound (EUS) technology to determine what cardiac structures could be assessed. This may be potentially beneficial during hemodynamic emergencies in the endoscopy suite resulting from hypovolemia, depressed ventricular function, aortic dissection, pericardial effusions, or aortic stenosis. Of the 20 patients enrolled, 18 underwent EUS with a linear echoendoscope for standard clinical indications followed by a cardiac assessment performed under the guidance of a TEE-certified cardiacanesthesiologist. Eight of the 20 standard views of cardiovascular structures per the 1999 American Society of Echocardiography/Society of Cardiovascular Anesthesiologists guidelines for TEE could be obtained using the linear echoendoscope. The following cardiac valvular structures were visualized: aortic valve (100%), mitral valve (100%), tricuspid valve (33%), and pulmonic valve (11%). Left ventricular and right ventricular systolic function could be assessed in 89% and 67% of patients, respectively. Other structures such as the ascending and descending aorta, pericardium, left atrial appendage, and interatrial septum were identified in 100% of patients. Doppler-dependent functions could not be assessed. Given that the EUS images were not directly compared with TEE in these patients, we cannot comment definitively on the quality of these assessments and further studies would need to be performed to make a formal comparison. Based on this study, EUS technology can consistently assess the mitral valve, aortic valve, aorta, pericardium, and left ventricular function. Given its

limitations, EUS technology, although not a substitute for formal echocardiography, could be a helpful early diagnostic tool in an emergency setting.

用於電休克治療的琥珀醯膽鹼及羅庫溴銨的最小有效劑量：一項前瞻性隨機交叉研究

Effective Doses of Succinylcholine and Rocuronium During Electroconvulsive Therapy: A Prospective, Randomized, Crossover Trial

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背景：電休克治療（electroconvulsive therapy，ECT）期間需要應用肌松藥以控制過度的肌肉收縮。在一項評估者設盲的前瞻性隨機交叉研究中，我們探討了用於電休克治療的琥珀醯膽鹼及羅庫溴銨的最小有效劑量（minimum effective dose, MED）。MED 是指為誘發抽搐過程中控制肌松達可接受程度提供預先的定量評估的最低劑量。

方法：琥珀醯膽鹼（0.8mg/kg）或者羅庫溴銨（0.4mg/kg）隨機用於接受 227 次電休克治療的 45 名患者。根據兩位元精神科專家（設盲）對肌肉收縮控制程度（充分、不充分或者過度鬆弛）的評估結果（可接受或不能接受）逐漸增加或者減少 10%的藥物劑量。定量監測神經肌肉傳遞功能直至肌松完全恢復。

結果：使得 50%的電休克治療患者產生可接受的肌松程度的琥珀醯膽鹼及羅庫溴銨的最低有效劑量（$MED50_{ECT}$）分別為 0.85mg/kg(95%置信區間 0.77-0.94)和 0.41mg/kg(95%置信區間 0.36-0.46)，而 90%的患者產生可接受的肌松程度的琥珀醯膽鹼及羅庫溴銨的最低有效劑量（$MED90_{ECT}$）分別為 1.06mg/kg(95%置信區間 1.0-1.27)和 0.57mg/kg(95%置信區間 0.5-0.6)。使用琥珀醯膽鹼和羅庫溴銨達到可接受的肌松程度時對應的肌顫搐高度分別為 0%（0-4）和 4%（0-30；$p<0.01$），而肌松恢復時間分別為 9.7±3.5 分鐘和 19.5±5.7 分鐘。

結果：電休克治療需要抑制 90%的肌顫搐已到達控制肌肉收縮的目的。琥珀醯膽鹼的首次劑量應該根據每一位元患者的術前情況而定，0.77-1.27mg/kg 範圍內的琥珀醯膽鹼可使 50%-90%電休克治療患者達到可接受的肌松程度。當然，在肌松監測條件下適當劑量的羅庫溴銨（0.36-0.6mg/kg）-新斯的明組合也是一個合適的選擇。

（王之遙 譯 薛張綱 校）

BACKGROUND: Neuromuscular blockade is required to control excessive muscle contractions during electroconvulsive therapy (ECT). In a crossover, assessor-blinded, prospective randomized study, we studied the minimum effective dose (MED) of succinylcholine and rocuronium for ECT. The MED was the lowest dose to provide a predefined qualitative measure of acceptable control of muscle strength during induced convulsions。

METHODS: Succinylcholine (0.8 mg kg) or rocuronium (0.4 mg kg) was randomly administered in 227 ECT sessions to 45 patients. The dose was incrementally increased or decreased by 10% based on 2 psychiatrists' (blinded to treatment) assessment of "acceptable" or "not acceptable" control of evoked muscle contractions (sufficient versus insufficient or excessive paralysis). The neuromuscular transmission was monitored quantitatively until full recovery.

RESULTS: In our study, the MEDs of succinylcholine and rocuronium to produce

acceptable ECT conditions in 50% of patients (MED50ECT) were 0.85 mg kg (95% confidence interval [CI], 0.77-0.94) and 0.41 mg kg (95% CI, 0.36-0.46) and in 90% of patients (MED90ECT) were 1.06 mg kg (95% CI, 1.0-1.27) and 0.57 mg kg (95% CI, 0.5-0.6), respectively. Nadir twitch height for acceptable muscle activity was 0% (0-4) and 4% (0-30; P < 0.001), respectively, and the time to recovery of the neuromuscular transmission was 9.7 ± 3.5 and 19.5 ± 5.7 minutes, respectively.
CONCLUSIONS: A twitch suppression of >90% is needed for control of motor contractions during ECT. The initial ECT dose of succinylcholine should be selected based on each patient's preprocedural condition, ranging between 0.77 and 1.27 mg kg to produce acceptable muscle blockade in 50% to 90% of patients. Rocuronium-neostigmine combination is a safe alternative if appropriately dosed (0.36-0.6 mg kg) and monitored.

利多卡因削弱老年人皮膚成纖維細胞的增殖和生物合成功能

Lidocaine Impairs Proliferative and Biosynthetic Functions of Aged Human Dermal Fibroblasts

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背景：老年人面臨著術後傷口癒合併發症發生率增高的風險。因為局部麻醉藥經常滲透到外科傷口的真皮層中，我們想證實局部麻醉藥是否對成纖維細胞的增殖和生物合成功能有負性作用。胰島素樣生長因數 1(IGF-1)和轉化生長因數 β1 (TGF-β1)這類生長因數對傷口癒合有重要調節作用，所以我們還評估了局部麻醉藥對其影響。

方法：老年和青年志願者捐獻的人真皮成纖維細胞(HFB)暴露在臨床所使用濃度的局部麻醉藥中。我們比較了利多卡因、布比卡因、馬比弗卡因和羅呱卡因對 HFB 的影響，其中利多卡因對不利影響最大。然後我們評估了利多卡因對生長因數 IGF-1 和 TGF-β1 表達和功能的影響。最後，我們分別將 IGF-1 或 TGF-β1 同時分別暴露在利多卡因中，來評估他們對增殖和真皮膠原纖維的影響。

結果：利多卡因和馬比弗卡因抑制了老年人 HFB 的增殖（利多卡因為對照組的 88%，95%CI, 80%–98%, P = .009; 馬比弗卡因為對照組的 90%，95% CI, 81%–99%, P = .032），但在年輕人的 HFB 中並沒有發現此現象。羅呱卡因和布比卡因對增殖並無抑制作用。因為利多卡因的臨床作用與馬比弗卡因相似，再此我們僅關注利多卡因。利多卡因對老年人 HFB 的增殖的抑制作用可被 IGF-1 抵消。利多卡因抑制了老年捐獻者成纖維細胞中的 IGF-1 複製和胰島素樣生長因數受體(IGF1R) (IGF-1, log2 fold-change −1.25 [為對照組 42%, 95% CI, 19%–92%, P = .035] ；IGF1R, log2 fold-change −1.00 [為對照組 50%, 95% CI, 31%–81%, P = .014])。另一方面，利多卡因並不影響年輕人 HFB 中 GF-1 或 IGF1R 的轉錄物。暴露於利多卡因之後，無論是老年人還是年輕人 HFB，膠原 III 的轉錄物都有所下降(老年人 HFB log2 fold-change −1.28 [41% of control, 95% CI, 20%–83%, P = .022]；年輕人 HFB log2 fold-change −1.60 [33% of control, 95% CI, 15%–73%, P = .019])。而膠原 I 的轉錄物僅在老年人 HFB 中有所下降(log2 fold-change −1.82 [28% of control, 95% CI, 14%–58%, P = .006])。與轉錄物相似，利多卡因同樣同時抑制了年輕人和老年人 HFB 中膠原 III 的蛋白表達(年輕人 HFB log2 fold-change −1.79 [對照組的 29%, 95% CI, 18%–47%, P = .003]；老年人

HFB log2 fold-change −1.76 [對照組的 30%, 95% CI, 9%–93%, P = .043])。在年輕人和老年人 HFB 中，利多卡因對膠原 III 蛋白表達的作用都會被 TGF-β1 消除。**結論**：我們的結果表明利多卡因抑制了老年人 HFB 真皮修復的過程。利多卡因這種負性作用部分是因為與 IGF-1 和 TGF-β1 的相互作用。
（方婕 譯 薛張綱 校）

BACKGROUND: The aged are at increased risk of postoperative wound healing complications. Because local anesthetics are infiltrated commonly into the dermis of surgical wounds, we sought to determine whether local anesthetics adversely affect proliferative and biosynthetic functions of dermal fibroblasts. We also evaluated the effect of local anesthetics on insulin- like growth factor-1 (IGF-1) and transforming growth factor-β1 (TGF-β1), growth factors that are important regulators of wound healing.
METHODS: Human dermal fibroblasts (HFB) from aged and young donors were exposed to local anesthetic agents at clinically relevant concentrations. We screened the effects of lidocaine, bupivacaine, mepivacaine, and ropivacaine on proliferation of HFB. Lidocaine was most detrimental to proliferation in HFB. We then evaluated the effect of lidocaine on expression and function of the growth factors, IGF-1 and TGF-β1. Lastly, concurrent exposure to lidocaine and IGF-1 or TGF-β1 was evaluated for their effects on proliferation and expression of dermal collagens, respectively.
RESULTS: Lidocaine and mepivacaine inhibited proliferation in aged HFB (for lidocaine 88% of control, 95% confidence interval [CI], 80%–98%, P = .009 and for mepivacaine 90% of control, 95% CI, 81%–99%, P = .032) but not in young HFB. Ropivacaine and bupivacaine did not inhibit proliferation. Because of the clinical utility of lidocaine relative to mepivacaine, we focused on lidocaine. Lidocaine decreased proliferation in aged HFB, which was abrogated by IGF-1. Lidocaine inhibited transcripts for IGF-1 and insulin-like growth factor-1 receptor (IGF1R) in fibroblasts from aged donors (IGF-1, log2 fold-change −1.25 [42% of control, 95% CI, 19%–92%, P = .035] and IGF1R, log2 fold-change −1.00 [50% of control, 95% CI, 31%–81%, P = .014]). In contrast, lidocaine did not affect the expression of IGF-1 or IGF1R transcripts in the young HFB. Transcripts for collagen III were decreased after lidocaine exposure in aged and young HFB (log2 fold-change −1.28 [41% of control, 95% CI, 20%–83%, P = .022] in aged HFB and log2 fold-change −1.60 [33% of control, 95% CI, 15%–73%, P = .019] in young HFB). Transcripts for collagen I were decreased in aged HFB (log2 fold-change −1.82 [28% of control, 95% CI, 14%–58%, P = .006]) but not in the young HFB. Similar to the transcripts, lidocaine also inhibited the protein expression of collagen III in young and aged HFB (log2 fold-change −1.79 [29% of control, 95% CI, 18%–47%, P = .003] in young HFB and log2 fold-change −1.76 [30% of control, 95% CI, 9%–93%, P = .043] in aged HFB). The effect of lidocaine on the expression of collagen III protein was obviated by TGF-β1 in both young and aged HFB.
CONCLUSIONS: Our results show that lidocaine inhibits processes relevant to dermal repair in aged HFB. The detrimental responses to lidocaine are due, in part, to interactions with IGF-1 and TGF-β1.

從麻醉住院醫生的視角在急救手冊的使用期間處理實際關鍵事件和安全文化的變化:一個試點研究

Emergency Manual Uses During Actual Critical Events and Changes in Safety Culture From the Perspective of Anesthesia Residents: A Pilot Study

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背景：急救手冊(EMs),認知幫助或危機列表背景相關的場景,已經在高度危險行業被使用了數十年, 儘管這是一個在醫療衛生方面新生的領域。2012 年秋天,斯坦福大學臨床推出急救手冊,包括掛在斯坦福手術室(ORs)和用來培訓臨床醫生使用的手術室的體格檢查及其理由。雖然模擬研究表明，使用的手術室團隊在危機期間使用的環境和類似的工具的有效性，但是完全沒有資料表明臨床上的實現和使用。在臨床使用者的一個子集(麻醉住院醫生),這個試點研究的目標是(1)在具有當地性手術室安全文化評估的觀點在使用急救手冊前前後關於認知援助的改變,雖然住院醫生已經在長期的模擬培訓背景;和(2) 描述在早期臨床關鍵事件中使用急救手冊。

方法：調查收集的定量和定性資料被用來評估在手術室臨床使用急救手冊。在 2011 年中期調查實施前斯坦福大學麻醉住院醫師已經接收到（相關性）郵件,其次是在 2014 年初調查實施後新的一批新住院意思（接受問卷調查）。實現後的調查包括探索性比較是否有調查問題和其他問題對於實現混合方法描述性分析,培訓和臨床使用過程中關鍵事件以來實現。

結果：(住院醫師)在調查前後反應率對比分別為 52%和 57%。在比較有調查試點研究後,更多住院醫師：同意或強烈同意“我工作所在的手術室在我工作時適當的提供諮詢急救的援助，”（ 73.8%, n = 31 vs 52.9%, n = 18, P = .0017）和選擇更多類型的麻醉專業“在一定程度上利用認知愛滋病，”（的醫師）包括訓練有素的麻醉醫師（z = −2.151, P = .0315）。在 15 個月後臨床推行急救手冊，19 個受訪者（45%）已經使用了急救手冊（運用到）一個實際的關鍵事件，而其中的 15 個人（78.9%）同意或非常同意在（手術室）期間“急救手冊幫助團隊能夠更好照顧病人”。我們目前的定性資料有 16 個來自 19 個急救手冊的從在以下領域的自由文本的使用報告：（1）啟動緊急手冊的使用，（2）閱讀使用方法，（3）診斷和治療，（4）病人護理的影響，和（5）急救手冊使用的障礙。

結論：自 2012 年斯坦福大學的臨床推行使用急救手冊,許多住院醫生在臨床關鍵事件中自述成功使用急救手冊。雖然這些報告都來自一個單一的機構的一項試驗性研究，他們作為一個早期的概念證明了臨床使用的可行性。未來需要大型，混合方法的研究來更好理解急救使用者及所面臨的困難以確定普遍性。

（童頡 譯 薛張綱 校）

BACKGROUND: Emergency manuals (EMs), context-relevant sets of cognitive aids or crisis checklists, have been used in high-hazard industries for decades, although this is a nascent field in health care. In the fall of 2012, Stanford clinically implemented EMs, including hanging physical copies in all Stanford operating rooms (ORs) and training OR clinicians on the use of, and rationale for, EMs. Although simulation studies have shown the effectiveness of EMs and similar tools when used by OR teams during crises, there are little data on clinical implementations and uses. In a subset of clinical users (ie, anesthesia residents), the objectives of this pilot study were to (1) assess perspectives on local OR safety culture regarding cognitive aid use before and after a systematic clinical implementation of EMs, although in the context of long-standing resident simulation trainings; and (2) to describe early clinical uses of EMs during critical events.

METHODS: Surveys collecting both quantitative and qualitative data were used to assess clinical adoption of EMs in the OR. A pre-implementation survey was e-mailed

to Stanford anesthesia residents in mid-2011, followed by a post-implementation survey to a new cohort of residents in early 2014. The post-implementation survey included pre-implementation survey questions for exploratory comparison and additional questions for mixed-methods descriptive analyses regarding EM implementation, training, and clinical use during critical events since implementation.
RESULTS: Response rates were similar for the pre- and post-implementation surveys, 52% and 57%, respectively. Comparing post- versus pre-implementation surveys in this pilot study, more residents: agreed or strongly agreed "the culture in the ORs where I work supports consulting a cognitive aid when appropriate" (73.8%, n = 31 vs 52.9%, n = 18, P = .0017) and chose more types of anesthesia professionals that "should use cognitive aids in some way," including fully trained anesthesiologists (z = −2.151, P = .0315). Fifteen months after clinical implementation of EMs, 19 respondents (45%) had used an EM during an actual critical event and 15 (78.9% of these) agreed or strongly agreed "the EM helped the team deliver better care to the patient" during that event, with the rest neutral. We present qualitative data for 16 of the 19 EM clinical use reports from free-text responses within the following domains: (1) triggering EM use, (2) reader role, (3) diagnosis and treatment, (4) patient care impact, and (5) barriers to EM use.
CONCLUSIONS: Since Stanford's clinical implementation of EMs in 2012, many residents' selfreport successful use of EMs during clinical critical events. Although these reports all come from a pilot study at a single institution, they serve as an early proof of concept for feasibility of clinical EM implementation and use. Larger, mixed-methods studies will be needed to better understand emerging facilitators and barriers and to determine generalizability.

麻醉相關的一氧化碳接觸：毒性和潛在的治療作用

Anesthesia-Related Carbon Monoxide Exposure: Toxicity and Potential Therapy

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通過二氧化碳吸收劑和體內重複呼吸產生的一氧化碳，揮發性麻醉藥的降解會導致全身麻醉過程中暴露於一氧化碳。儘管遵守 the Anesthesia Patient Safety Foundation 的指南可以減少一氧化碳中毒的風險，患者在低流量吸入麻醉時仍然可能暴露於亞毒性一氧化碳下。這種結果相對來說比較不為人所知。與廣為人知的高濃度一氧化碳的毒性對比，低濃度一氧化碳的生物學活性最近已證明是具有細胞保護作用的。因此，低劑量的一氧化碳正在被探討作為治療各種不同的疾病的一種新型方案。我們要在這篇文章複習與麻醉有關的一氧化碳暴露的概念，確定其產生的來源，明確一氧化碳公開毒性的機制，突出低劑量一氧化碳的細胞作用，討論一氧化碳作為常規麻醉管理部分的潛在

（李桂婷 譯 薛張綱 校）

Exposure to carbon monoxide (CO) during general anesthesia can result from volatile anesthetic degradation by carbon dioxide absorbents and rebreathing of endogenously produced CO. Although adherence to the Anesthesia Patient Safety Foundation guidelines reduces the risk of CO poisoning, patients may still experience subtoxic CO exposure during low-flow anesthesia. The consequences of such exposures are relatively unknown. In contrast to the widely recognized toxicity of high CO concentrations, the biologic activity of low concentration CO has recently been shown to be cytoprotective. As such, low-dose CO is being explored as a novel treatment for a variety of different diseases. Here, we review the concept of

anesthesia-related CO exposure, identify the sources of production, detail the mechanisms of overt CO toxicity, highlight the cellular effects of low-dose CO, and discuss the potential therapeutic role for CO as part of routine anesthetic management.

血管加壓素和催產素對雙灌注、單一的、分離子葉的胎兒胎盤遠端幹動脈血管阻力的影響

The Effects of Vasopressin and Oxytocin on the Fetoplacental Distal Stem Arteriolar Vascular Resistance of the Dual-Perfused, Single, Isolated, Human Placental Cotyledon

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背景：血管活性藥物用於糾正剖腹產時低血壓，理論上會加劇低氧胎兒胎盤血管收縮反應，因此，也會對經胎兒胎盤氧供產生負面影響。但是，這方面的藥效學資料很少提到，更別說調查了。血管加壓素，一種強效的全身血管收縮劑。催產素，剖腹產中常規用的子宮收縮劑，與血管加壓素相比，具有顯著的舒張全身血管的性質，我們假設其不會影響到遠端幹絨毛小動脈阻力。

方法：人胎盤灌注模型雙灌注、單一的，分離的子葉，被用來研究從健康婦女獲得的胎盤中胎兒胎盤迴圈阻力對催產素和血管加壓素的反應。共 17 個研究物件的 12 個被成功的將催產素或血管加壓素引入到胎兒儲層中，以 10-1M 的增加濃度。胎兒胎盤遠端幹絨毛動脈灌注壓（FAP）被連續測量。催產素或者加壓素的胎兒回路濃度以逐步的方式分別從 10-9 到 10−5 M 或 10−11 到 10−6 M。兩種儲層被藥物淨化後，1-mL 1.0 mM5-羥色胺(2.5 μM)被引入到胎兒回路中，眾所周知，5-羥色胺可以顯著增加胎兒胎盤遠端幹絨毛動脈阻力。暴露於 5-羥色胺，FAP 從基線上的顯著增加證實了胎兒胎盤收縮反應保持活性。本實驗的主要結果是加壓素和催產素劑量增加時 FAP 的變化。

結果：無論是催產素還是加壓素，無論哪個藥物試驗濃度，都沒有觀察到 FAP 變化。對於每一種藥物和每一種濃度，大於±10 mm Hg 的平均壓變化在 95%的置信區間都被排除在外。相比之下，5-羥色胺在 12 個成功的試驗中能顯著增加灌注壓。

結論：催產素和加壓素不影響人胎兒胎盤遠端幹絨毛動脈阻力。在此注意到的加壓素無影響類似於報導過的對人肺動脈阻力的影響，微不足道。兩種藥物似乎都不能對低氧血症胎兒胎盤收縮反應代償產生不利影響。

（李倩倩 譯 薛張綱 校）

BACKGROUND: Vasoactive agents administered to counter maternal hypotension at cesarean delivery may theoretically intensify the hypoxemic fetoplacental vasoconstrictor response and, hence, negatively impact transplacental oxygen delivery to the fetus. Yet, this aspect of their pharmacodynamic profiles is seldom mentioned, let alone investigated. We hypothesized that vasopressin, a potent systemic vasoconstrictor, and oxytocin, a uterotonic agent administered routinely at cesarean delivery, which, in contrast to vasopressin, possesses significant systemic vasodilator properties, would not influence distal stem villous arteriolar resistance.

METHODS: The dual-perfused, single, isolated cotyledon, human placental perfusion model was used to examine the resistance response of the fetoplacental

circulation to oxytocin and vasopressin in placentae harvested from healthy women. Twelve of a total of 17 individual experiments were conducted successfully during which either oxytocin (n = 6) or vasopressin (n = 6) was introduced into the fetal reservoir in concentration increments of 10^{-1} M. Fetoplacental distal stem villous arteriolar perfusion pressure (FAP) was measured continuously. The fetal circuit concentration of either oxytocin or vasopressin was raised in a stepwise fashion from 10^{9} to 10^{-5} M or 10^{-11} to 10^{-6} M, respectively. Both reservoirs were then purged of drug, after which 1-mL 1.0 mM 5-hydroxytryptamine (2.5 μM), an agent well known to manifestly increase fetoplacental distal stem villous arteriolar resistance, was introduced into the fetal circuit. A significant increase in FAP from baseline in response to exposure to 5-hydroxytryptamine confirmed that the fetoplacental vasoconstrictor response remained reactive. The primary outcome of this study was changes in FAP after incremental dosing of vasopressin and oxytocin.

RESULTS: No changes in FAP were observed with either oxytocin or vasopressin regardless of the drug concentration tested. For each drug and concentration, a mean pressure change greater than ±10 mm Hg was excluded with 95% confidence. In contrast, 5-hydroxytryptamine significantly increased perfusion pressure in all 12 successful experiments.

CONCLUSIONS: Oxytocin and vasopressin do not influence human fetoplacental distal stem villous arteriolar resistance. The neutral impact of vasopressin noted here is thus analogous to the reported negligible influence of the drug on human pulmonary arteriolar resistance. Neither drug seems likely to adversely influence the compensatory hypoxemic fetoplacental vasoconstrictor response.

未經修復的法洛四聯症相關病理生理學改變減少了患兒對依託醚酯的系統清除率

Unrepaired Tetralogy of Fallot-related Pathophysiologic Changes Reduce Systemic Clearance of Etomidate in Children

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背景：先天性心臟病兒童的病理生理學改變可能通過影響藥代動力學（PK）而改變藥物的效果。考慮到描述兒科患者藥代動力學的文獻很有限，尤其是那些有法洛四聯症（TOF）的患者，我們的目標是描繪依託醚酯的藥代動力學，並且探索 TOF 對其的影響。

方法：29 名在全麻下行擇期外科手術的兒科患者（15 名 TOF 患兒，14 名正常心臟解剖患兒）被納入本次研究。在麻醉誘導期間所有患兒靜脈使用了 60μg/kg/min 的依託醚酯，直到 BIS 值≤50 持續 5 秒。動脈血標本被抽取並且分析了。我們用了 NONMEM 軟體來進行人口學分析以定義 PK 特徵。

結果：從平均年齡為 236 天（從 86-360 天）的 29 名兒童中收取了 244 個標本資料，包括平均年齡為 221 天（從 86-360 天）的 TOF 組及平均年齡 221 天（從 86-360 天）的心臟解剖結構正常組。我們發現用三室分佈模型來描述依託醚酯的 PK 是最合適的。TOF 的引入作為一個系統清除率（Cl1）的協變數優化了這個模型並且導致了目標函數的顯著縮減（Δ 目標函數= -7.33; P = .0068），這意味著 TOF 是 Cl1 的一個重要協變數，TOF 兒童的依託醚酯 Cl1 值(1.67 × (體重

[WT]/70 kg) L/min) 低於心臟解剖結構正常的患者的 Cl1 值（2.28 × (WT/70 kg) L/min）。其他 PK 參數值如下：V1 = 8.05 × (WT/70 kg) L; V2 = 13.7 × (WT/70 kg) L; V3 = 41.3 × (WT/70 kg) L; Cl2 = 3.35 × (WT/70 kg) L/min; Cl3 = 0.563 × (WT/70 kg) L/min。

總結：TOF 患兒的依託醚酯清除率的減少導致了比起正常兒童，只需更低的注射速度以及更短的注射時間便可達到相同的血漿濃度並且維持一個平衡的目標濃度，或者在單次劑量或持續注射後有更長的鎮靜時間以及恢復時間。

（黃慧芸 譯 薛張綱 校）

BACKGROUND：Pathophysiologic changes in children with congenital heart disease may alter the effect of drugs by influencing the pharmacokinetics (PK). Considering the limited literature that describes the PK of etomidate in pediatric patients, especially in those with tetralogy of Fallot (TOF), our aim was to characterize the PK of etomidate and explore the effects of TOF.

METHODS: Twenty-nine pediatric patients (15 with TOF and 14 with normal cardiac anatomy) scheduled to undergo elective surgery under general anesthesia were recruited in the study. All children received etomidate 60 μg/kg/min intravenously until a bispectral index of ≤50 was reached for 5 seconds during anesthesia induction. Arterial blood samples were drawn and analyzed. Population analysis was performed by using NONMEM to define PK characteristics. The estimates were standardized to a 70-kg adult using a per-kilogram model.

RESULTS: Data consisting of 244 samples from 29 children with a mean age of 236 days (range, 86-360 days) were used, including a TOF group with a mean age of 250 days (range, 165-360 days) and a normal cardiac anatomy group with a mean age of 221 days (range, 86-360 days). A 3-compartment disposition model was best fitted to describe the PK of etomidate. The introduction of TOF as a covariate for systemic clearance (Cl1) improved the model and resulted in a significant reduction of objective function (Δobjective function = -7.33; P = .0068), which means that TOF was a significant covariate of Cl1, and the etomidate Cl1 in children with TOF (1.67 × (weight [WT]/70 kg) L/min) was lower than those with normal cardiac anatomy (2.28 × (WT/70 kg) L/min). Other PK parameter values were as follows: V1 = 8.05 × (WT/70 kg) L; V2 = 13.7 × (WT/70 kg) L; V3 = 41.3 × (WT/70 kg) L; Cl2 = 3.35 × (WT/70 kg) L/min; Cl3 = 0.563 × (WT/70 kg) L/min.

CONCLUSIONS: A decreased systemic clearance for etomidate in children with TOF resulted in a lower required infusion rate and variation with time to achieve the same plasma concentration and maintain an equivalent target concentration or have longer sedation and recovery times after bolus or continuous infusion than normal children.

在神經病理性疼痛模型中，奈福泮的抗痛覺超敏作用可被三磷酸腺苷敏感的鉀離子通道調停

The Antiallodynic Effects of Nefopam Are Mediated by the Adenosine Triphosphate–Sensitive Potassium Channel in a Neuropathic Pain Model

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背景：在神經病理性疼痛模型中，奈福泮在鎮痛和抗痛覺超敏作用上起著核心作用。以往的研究已經證實，三磷酸腺苷敏感的鈣離子通道的啟動可以起到抗

神經病理性疼痛中痛覺超敏的作用。在這項研究中，我們探索了鉀離子通道和奈福泮的關係，來證實在神經病理性疼痛模型中，是否鉀離子通道可以調停奈福泮的抗痛覺超敏作用。

方法：機械性痛覺超敏可以在脊神經結紮的鼠中被誘發出來。所有鼠的縮足反應閾值通過馮弗雷纖維刺激來評估。在實驗鼠脊神經結紮前後分別腹腔內給予奈福泮。我們評估了奈福泮和鞘內注射 KCa^{2+} 通道抑制劑—蜂毒明肽、卡律蠍毒素，和 KATP 通道阻滯劑格列本脲來評估它們逆轉奈福泮抗痛覺超敏的能力。除此之外，我們還要評估是否 KATP 通道開放劑吡那地爾有抗痛覺超敏作用和促進奈福泮的抗痛覺超敏的作用。

結果：在實驗鼠脊神經結紮前後給予奈福泮可引出顯著的抗痛覺超敏的作用 ($P < .01$)，在給予格列本脲也出現了顯著的抗痛覺超敏作用 ($P < .01$)。吡那地爾可提高奈福泮的抗痛覺超敏作用 ($P < .01$)。然而蜂毒明肽、卡律蠍毒素對奈福泮的抗痛覺超敏幾乎無作用。

結論： KATP 通道激動劑可使奈福泮的抗痛覺超敏作用增加，而 KATP 通道抑制劑可逆轉奈福泮的抗痛覺超敏作用。這些資料都說明了在神經病理性疼痛模型中，KATP 通道參與了奈福泮的抗痛覺超敏作用。

（李祥婷 譯 薛張綱 校）

BACKGROUND: Nefopam hydrochloride is a centrally acting compound that induces antinociceptive and antihyperalgesic properties in neuropathic pain models. Previous reports have shown that activation of adenosine triphosphate (ATP)-sensitive and calcium-activated potassium (K_{ATP} and K_{Ca2+}) channels has antiallodynic effects in neuropathic pain. In the present study, we evaluated the relationship between potassium channels and nefopam to determine whether the antiallodynic effects of nefopam are mediated by potassium channels in a neuropathic pain model.

METHODS: Mechanical allodynia was induced by spinal nerve ligation (SNL) in rats, and the paw withdrawal threshold (PWT) was evaluated by the use of von Frey filaments. Nefopam was administered intraperitoneally before or after SNL. We assessed the relationship between nefopam and intrathecal injection of the K_{Ca2+} channel antagonists apamin and charybdotoxin, and the K_{ATP} channel blocker glibenclamide to assess their abilities to reverse the antiallodynic effects of nefopam. In addition, we evaluated whether the K_{ATP}channel opener pinacidil had antiallodynic effects and promoted the antiallodynic effects of nefopam.

RESULTS: Administration of nefopam before and after SNL induced significant antiallodynic effects ($P < .01$, respectively), which were significantly reduced by glibenclamide ($P < .01$). Pinacidil improved the antiallodynic effects of nefopam ($P < .01$); however, apamin and charybdotoxin had little effects on the antiallodynic properties of nefopam.

CONCLUSIONS: The antiallodynic effects of nefopam are increased by a K_{ATP} channel agonist and reversed by a K_{ATP} channel antagonist. These data suggest that the K_{ATP}channel is involved in the antiallodynic effects of nefopam in a neuropathic pain model.

走向平衡的一步：凝血因數聯合抗凝血酶補充能夠促進凝血酶生成
A Step Toward Balance: Thrombin Generation Improvement via Procoagulant

Factor and Antithrombin Supplementation

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背景：在創傷及手術引起的凝血功能障礙情況下應用凝血酶原複合物可能伴發血栓栓塞的不良事件。本次試驗通過建立血漿稀釋模型，在其中單獨或聯合加入 3-4 種因數的凝血酶原複合物、抗凝血酶或重組凝血因數Ⅶ，以研究其在促進血栓形成（TG）中的作用，同時構建電腦模型並檢驗其能否預測在治療稀釋性凝血障礙患者時的 TG 情況。

方法：研究者運用自動校正凝血酶曲線法分別對 10 名健康志願者的未稀釋血漿，3 倍生理鹽水稀釋血漿，稀釋血漿中加入重組凝血因數 VII（rFVIIa 組），加入凝血因數 II,IX,X 和抗凝血酶（CCF-AT 組），加入凝血因數 II,VII,IX,X（CCF-FVII 組）進行凝血酶試驗。同時本次研究根據現有凝血酶生成電腦模型，在其中加入影響自動校正凝血酶曲線法結果的因素，並利用不同凝血酶試驗資料進行建模和模型檢驗。

結果：rFVIIa 組較其稀釋前水準，明顯縮短凝血酶形成的峰值和延遲時間（P<0.001），但無法恢復正常凝血酶峰值（P<0.001）。CCF-FVII 組在較其稀釋前水準，明顯縮短凝血酶形成的峰值時間(P < 0.001)和延遲時間(P = 0.034)，同時增加凝血酶峰值和內源性凝血酶潛能。CCF-AT 組能夠促進凝血酶生成，同時不影響凝血因數 VII 和 CCF-FVII 的作用。CCF-AT 組與加入 rFVIIa 的 CCF-FVII 組相比，分別在延遲時間（(P < 0.001 和 P = 0.005)，凝血酶形成的峰值時間（P < 0.001 和 P = 0.004），速率（P < 0.001 和 P = 0.019），凝血酶峰值（兩組均 P < 0.001）和內源性凝血酶潛能（P = 0.034 和 P = 0.019）上存在差異。本研究構建的模型能夠個體差異性地進行預測和描述治療後的凝血酶生成的促進效果。

結論：在稀釋血漿中，與單獨使用重組凝血因數 VII 和凝血因數 II,VII,IX,X 複合物相比，凝血因數 II,IX,X 和抗凝血酶複合物能夠更好促進凝血酶生成。同時本研究中構建的預測模型能夠指導進一步的血漿稀釋/因數補充實驗。

（吳瑋　譯　陳傑　校）

BACKGROUND: The use of prothrombin complex concentrates in trauma- and surgery-induced coagulopathy is complicated by the possibility of thromboembolic events. To explore the effects of these agents on thrombin generation(TG), we investigated combinations of coagulation factors equivalent to 3- and 4-factor prothrombin complex concentrates with and without added antithrombin (AT), as well as recombinant factor VIIa (rFVIIa), in a dilutional model. These data were then used to develop a computational model to test whether such a model could predict the TG profiles of these agents used to treat dilutional coagulopathy.

METHODS: We measured TG in plasma collected from 10 healthy volunteers using Calibrated Automated Thrombogram. TG measurements were performed in undiluted plasma, 3-fold saline-diluted plasma, and diluted plasma supplemented with the following factors: rFVIIa (group rFVIIa); factors (F)II, FIX, FX, and AT (group "combination of coagulation factors" [CCF]-AT); or FII, FVII, FIX, and FX (group CCF-FVII). We extended an existing computational model of TG to include additional reactions that impact the Calibrated Automated Thrombogram readout. We developed and applied a computational strategy to train the model using only a subset of the obtained TG data and used the remaining data for model validation.

RESULTS: rFVIIa decreased lag time and the time to thrombin peak generation beyond their predilution levels ($P < 0.001$) but did not restore normal thrombin peak height ($P < 0.001$). CCF-FVII supplementation decreased lag time ($P = 0.034$) and thrombin peak time ($P < 0.001$) and increased both peak height ($P < 0.001$) and endogenous thrombin potential ($P = 0.055$) beyond their predilution levels. CCF-AT supplementation in diluted plasma resulted in an improvement in TG without causing the exaggerated effects of rFVIIa and CCF-FVII supplementation. The differences between the effects of CCF-AT and supplementation with rFVIIa and CCF-FVII were significant for lag time ($P < 0.001$ and $P = 0.005$, respectively), time to thrombin peak ($P < 0.001$ and $P = 0.004$, respectively), velocity index ($P < 0.001$ and $P = 0.019$, respectively), thrombin peak height ($P < 0.001$ for both comparisons), and endogenous thrombin potential ($P = 0.034$ and $P = 0.019$, respectively). The computational model generated subject-specific predictions andidentified typical patterns of TG improvement.
CONCLUSIONS: In this study of the effects of hemodilution, CCF-AT supplementation improved the dilution-impaired plasma TG potential in a more balanced way than either rFVIIa alone or CCF-FVII supplementation. Predictive computational modeling can guide plasma dilution/supplementation experiments.

心臟外科手術病人體外迴圈複溫時與離線後血栓彈力圖纖維蛋白原水準比較
Comparison of Thrombelastography-Derived Fibrinogen Values at Rewarming and Following Cardiopulmonary Bypass in Cardiac Surgery Patients

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背景：圍術期過度輸血的高成本與不良反應使得臨床工作者探究針對性凝血因數替代療法，其中備受關注的凝血因數之一是凝血因數 I（纖維蛋白原）。低纖維蛋白原血症可由標準實驗室檢測手段進行診斷，但相對費時。血小板抑制的全血血栓彈力圖（TEG）可檢測功能性纖維蛋白原水準（FLEV）並計算出纖維蛋白原含量，顯著縮短了檢測時間。若體外迴圈（CPB）複溫過程中與 CPB 停止後即刻 FLEV 值相似，則 CPB 複溫過程中的 FLEV 值可作為血製品輸注的預先評判指標。
方法：51 例心臟手術病人被納入此項前瞻性非隨機研究，採用 TEG FLEV 方法測定比較 CPB 複溫過程與 CPB 後纖維蛋白原水準。所有病人的基線、複溫過程與 CPB 後纖維蛋白原值通過傳統實驗室檢測（Clauss 法）和 FLEV 測得。運用混合效應回歸模型檢測 TEG FLEV 值的變化。Bland-Altman 法分析標準實驗室檢查與 FLEV 法之間的偏移和一致性範圍（LOA）。
結果：49 例患者被納入統計分析。複溫 FLEV 平均值為 333.9mg/dL，給予魚精蛋白後 FLEV 平均值為 332.8mg/dL，兩者差異-1.1mg/dL（95%可信區間〔CI〕，-25.8～23.6，P=0.917）。給予魚精蛋白後 FLEV 測值前平均 47 分鐘獲得複溫 FLEV 值。Bland-Altman 分析提示 FLEV 與標準測法存在較大差異，基線值平均相差 92.5mg/dL（95% CI，71.1～114.9），最低 LOA -56.5mg/dL（95% CI，-94.4～-18.6），最高 LOA 242.4mg/dL（95% CI，204.5～280.3）。兩種檢測方法的差別在 CPB 結束後更顯著並持續到給予魚精蛋白後。
結論：本研究提示 FLEV 值在複溫過程與 CPB 後無明顯變化，CI 區間變化無臨床意義。這些結果表明在 CPB 離線前可採用複溫樣本來指導纖維蛋白原特異性

治療。平均 FLEV 值在各時間點均高於傳統實驗室檢查測定值。另外，病例之間存在顯著異質性，提示在同一個病人運用不同檢測方法存在較大差異。（謝律　譯　陳傑　校）

BACKGROUND: The inflated costs and documented deleterious effects of excess perioperative transfusion have led to the investigation of targeted coagulation factor replacement strategies. One particular coagulation factor of interest is factor I (fibrinogen). Hypofibrinogenemia is typically tested for using time-consuming standard laboratory assays. The thrombelastography (TEG)-based functional fibrinogen level (FLEV) provides an assessment of whole blood clot under platelet inhibition to report calculated fibrinogen levels in significantly less time. If FLEV valuesobtained on cardiopulmonary bypass (CPB) during rewarming are similar to values obtained immediately after the discontinuation of CPB, thenrewarming values could be used for preemptive ordering of appropriate blood product therapy.

METHODS: Fifty-one cardiac surgery patients were enrolled into this prospective nonrandomized study to compare rewarming fibrinogen valueswithpostbypass values using TEG FLEV assays. Baseline, rewarming, and postbypass fibrinogen values were recorded for all patients using both standard laboratory assay (Clauss method) and FLEV. Mixed-effects regression models were used to examine the change in TEG FLEV valuesover time. Bland-Altman analysis was used to examine bias and the limits of agreement (LOA) between the standard laboratory assay and FLEVs.

RESULTS: Forty-nine patients were included in the analysis. The mean FLEV value during rewarming was 333.9 mg/dL compared with 332.8 mg/dL after protamine, corresponding to an estimated difference of -1.1 mg/dL (95% confidence interval [CI], -25.8 to 23.6; P = 0.917). Rewarmingvalues were available on average 47 minutes before postprotamine values. Bland-Altman analysis showed poor agreement between FLEV and standard assays: mean difference at baseline was 92.5 mg/dL (95% CI, 71.1 to 114.9), with a lower LOA of -56.5 mg/dL (95% CI, -94.4 to -18.6) and upper LOA of 242.4 mg/dL (95% CI, 204.5 to 280.3). The difference between assays increased after CPB and persisted after protamine administration.

CONCLUSIONS: Our results revealed negligible change in FLEV values from the rewarming to postbypass periods, with a CI that does not include clinically meaningful differences. These findings suggest that rewarming samples could be utilized for ordering fibrinogen-specific therapies before discontinuation of CPB. Mean FLEV values were consistently higher than the reference standard at each time point. Moreover, bias was highly heterogeneous among samples, implying a large range of potential differences between assays for any 1 patient.

比較靜脈注射和口服方式攝入撲熱息痛後藥物在血漿和腦脊液中的藥代動力學情況

Comparative Plasma and Cerebrospinal Fluid Pharmacokinetics of Paracetamol After Intravenous and Oral Administration

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背景：本研究比較了靜脈注射(IV)和口服方式攝入撲熱息痛後，藥物在血漿和腦脊液中的藥代動力學情況，目的為調整用藥以獲得最適腦脊液濃度。
方法：21 位成年患者隨機分三組：靜脈注藥 1g，口服給藥 1g，口服給藥 1.5g。分別留置靜脈導管和鞘內導管，給藥後 6h 內採集靜脈血和腦脊液標本。通過非房室模型技術分析血漿和腦脊液的最大藥物濃度（Cmax），達到最大藥物濃度的時間（Tmax），血漿和腦脊液的藥物濃度-時間曲線下面積（AUCs）。當 P < .0167 時有統計學意義（用 Bonferroni 法校正 3 次比較對應的參數值）。用 Bonferroni 校正 95%置信區間（CIs）（0.5 的置信區間是無效假設）來計算概率（X<Y）(P")。統計結果用中位數或 P"（置信區間）來表示。分別比較靜脈注藥 1g-口服給藥 1g，靜脈注藥 1g-口服給藥 1.5g，口服給藥 1g-口服給藥 1.5g，三組兩兩比較求出 P 值。
結果：撲熱息痛濃度在不同組中有較大差異，尤其是口服藥物組。靜脈注藥 1g 組的血漿 Cmax 中位數明顯高於口服給藥 1g 組。相反，兩組的腦脊液 Cmax 中位數無差異。靜脈注藥 1g 組的血漿 Tmax 中位數是 105min，比口服藥物 1g 和 1.5g 組提前 75min。而兩組的腦脊液 Tmax 中位數無明顯差異。血漿 AUC（總）中位數在兩組間無明顯差異；然而用藥第一個小時，靜脈注藥 1g 組血漿 AUC 中位數明顯高於口服給藥組。第二個小時兩組無差異。兩組的腦脊液 AUC（總）中位數無明顯差異；然而用藥第一個小時，靜脈注藥 1g 組腦脊液 AUC 中位數明顯高於口服藥組。第二個小時兩組無差異。由於樣本量太小，研究分析 Cmax、Tmax 和 AUC 中位數值缺乏精確性。
結論：靜脈注藥與口服藥物相比可達到更大的血漿濃度峰值，達峰時間更快。由於研究樣本量小，不同給藥方式對腦脊液的 Cmax 和 Tmax 影響並未顯示差異性。
（戴依利　譯　陳傑　校）
BACKGROUND: We compared plasma and cerebrospinal fluid (CSF) pharmacokinetics of paracetamol after intravenous (IV) and oral administration to determine dosing regimens that optimize CSF concentrations.
METHODS: Twenty-one adult patients were assigned randomly to 1 g IV, 1 g oral or 1.5 g oral paracetamol. An IV cannula and lumbar intrathecal catheter were used to sample venous blood and CSF, respectively, over 6 hours. The plasma and CSF maximum concentrations (C max), times to maximum concentrations (T max), and area under the plasma and CSF concentration-time curves (AUCs) were calculated using noncompartmental techniques. Significance was defined by P < .0167 (Bonferroni correction for 3 comparisons for each parameter). Probability (X < Y) (P〃) with Bonferroni corrected 95% confidence intervals (CIs) were calculated (CIs including 0.5 meet the null hypothesis). Results are presented as median (range) or P〃 (CI). P values are listed as 1 g IV vs 1 g orally, 1 g IV vs 1.5 g orally and 1 g orally vs 1.5 g orally, respectively.
RESULTS: Wide variation in measured paracetamol concentrations was observed, especially in the oral groups. The median plasma C max in the 1 g IV group was significantly greater than the oral groups. In contrast, the median CSF C maxwas not different between groups. The median plasma T max in the 1 g IV group was 105 and 75 minutes earlier than in the 1 and 1.5 g oral groups. The median CSF T max was not significantly different between groups. The median plasma AUC (total) was not significantly different between groups; however, in the first hour, the median plasma AUC was significantly greater in the IV group than in the oral groups. In the second hour, there was no difference between groups. The median CSF AUC (total) did not

significantly differ between groups; however, in the first hour, the median CSF AUC was significantly greater in the IV compared with the orally groups. In the second hour, there was no difference between groups. Our analysis indicated that the median C max, T max, and AUC values lacked precision because of small sample sizes.
CONCLUSIONS: Peak plasma concentrations were greater and reached earlier after IV than oral dosing. Evidence for differences in CSF C max and T max was lacking because of the small size of this study.

機械通氣對鎖骨下靜脈穿刺置管術中氣胸發生率的影響：一個前瞻性隨機的非劣效性試驗

Influence of Mechanical Ventilation on the Incidence of Pneumothorax During InfraclavicularSubclavian Vein Catheterization: A Prospective Randomized Noninferiority Trial

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背景：目前仍不清楚在鎖骨下靜脈穿刺置管術期間是否需要中斷機械通氣。在實踐中，由臨床醫生自己決定是否進行肺萎陷。本研究目的是評估機械通氣對鎖骨下靜脈穿刺置管術中氣胸發生率的影響。
方法：一共 332 名需要進行鎖骨下靜脈穿刺置管術的病人被隨機分配至：鎖骨下靜脈穿刺置管期間維持機械通氣（機械通氣組，n=165）或中斷機械通氣（肺萎陷組，n=167）。比較兩組氣胸和其他併發症如誤入動脈、血胸或導管移位以及穿刺置管成功率的差異。
結果：機械通氣組氣胸發生率為 0%（0/165），肺萎陷組 0.6%（1/167）。肺萎陷組氣胸發生率比機械通氣組高 0.6%，差異的雙側 90%可信區間為（-1.29%~3.44%），由於可信區間下限-1.29%比預先設定的非劣效性界限-3%高，在 0.05 顯著性水準下，機械通氣組比肺萎陷組更劣的假設被拒絕。兩組其他併發症發生率和穿刺置管成功率相似。肺萎陷組 9 名患者氧飽和度下降低於 95%，而機械通氣組則沒有發生（P=0.007）。
結論：不管是否進行機械通氣，鎖骨下靜脈穿刺置管術的成功率和併發症發生率相似。在置管術期間，中斷機械通氣對預防氣胸似乎並非必要。
（殷智宇 譯 陳傑 校）

BACKGROUND: It remains unclear whether we have to interrupt mechanical ventilation during infraclavicular subclavian venous catheterization. In practice, the clinicians' choice about lung deflation depends on their own discretion. The purpose of this study was to assess the influence ofmechanical ventilation on the incidence of pneumothorax during infraclavicular subclavian venous catheterization.
METHODS: A total of 332 patients, who needed subclavian venous catheterization, were randomly assigned to 1 of the 2 groups: catheterizations were performed with the patients' lungs under mechanical ventilation (ventilation group, n = 165) or without mechanical ventilation (deflation group, n = 167). The incidences of pneumothorax and other complications such as arterial puncture, hemothorax, or catheter misplacements and the success rate of catheterization were compared.
RESULTS: The incidences of pneumothorax were 0% (0/165) in the ventilation group and 0.6% (1/167) in the deflation group. The incidence of pneumothorax in the deflation group was 0.6% higher than that in the ventilation group and the 2-sided

90% confidence interval for the difference was (-1.29% to 3.44%). Because the lower bound for the 2-sided 90% confidence interval, -1.29%, was higher than the predefined noninferiority margin of -3%, the inferiority of the ventilation group over the deflation group was rejected at the .05 level of significance. Other complication rates and success rates of catheterization were comparable between 2 groups. The oxygen saturation dropped below 95% in 9 patients in the deflation group, while none in the ventilation group (P =0.007).
CONCLUSIONS: The success and complication rates were similar regardless of mechanical ventilation. During infraclavicular subclavian venous catheterization, interruption of mechanical ventilation does not seem to be necessary for the prevention of pneumothorax.

完全液體通氣誘發的短暫性低體溫減少主動脈阻斷誘發的靶器官損傷及多器官功能衰竭

A Brief Period of Hypothermia Induced by Total Liquid Ventilation Decreases End-Organ Damage and Multiorgan Failure Induced by Aortic Cross-Clamping
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背景：在動物模型中，心跳驟停和其他低灌注狀態發生後全身降溫可減少靶器官損傷。但是，可能由於長時間低體溫的不利影響可抵消任何潛在的好處，在人體中進行低體溫處理的獲益是不確定的。完全液體通氣（TLV）可同時提供超快降溫和複溫。先前報導，用 TLV 超快降溫可有效地降低心臟驟停後動物模型的神經損傷。本研究假設通過 TLV 快速降溫和複溫可以減輕主動脈阻斷引起的缺血再灌注後多器官功能衰竭（MOF）。
方法：對麻醉後家兔先行腹腔幹上腹主動脈阻斷 30min，隨後進行 300min 再灌注。分別在阻斷前，阻斷時和阻斷後進行常規通氣（對照組）或低溫 TLV（33℃）（分別為夾閉前組，夾閉組和夾閉後組）。所有 TLV 組，低溫持續 75min 後並在恢復常規機械通氣前切換到複溫模式。研究終點包括再灌注後 300min 檢測的心血管、腎臟、肝臟及炎症參數。
結果：在常溫（對照）組，缺血再灌注損傷引發 MOF 的證據包括嚴重血管麻痹、低心輸出量、急性腎損傷和肝功能衰竭。觀察到與對照組相比，TLV 組的心輸出量在夾閉後組、夾閉組和夾閉前組漸次改善（再灌注 300min 後分別為 53±8，64±12 和 90±24vs36±23 mL/min/kg）。預夾閉組和夾閉組的肝臟生物標誌物水準較對照組更低。然而，預夾閉組可預防急性腎損傷發生，預夾閉可將其控制在一定程度，但夾閉後組不可預防急性腎損傷。例如，預夾閉組和對照組在隨訪末肌酐清除率分別為 4.8±3.1 和 0.5±0.6 mL/kg/min（p =0.0004）。比較 TLV 組和對照組的心臟、腎臟、肝臟和空腸的組織學檢查也證實 TLV 可降低損傷。
結論：TLV 短暫超快降溫繼而快速複溫可以減弱主動脈阻斷後多器官功能衰竭生化和病理指標。即使再灌注後實施短暫低溫 TLV，也可減輕心血管和肝功能障礙。相反，只有再灌注前進行降溫才能限制急性腎損傷。需要進一步研究以確定該實驗結果的臨床意義，並確定 TLV 誘導低溫對低灌注狀態終末器官保護

的最佳持續時間和時機。
(陳依 譯 陳傑　校)

BACKGROUND: In animal models, whole-body cooling reduces end-organ injury after cardiac arrest and other hypoperfusion states. The benefits of cooling in humans, however, are uncertain, possibly because detrimental effects of prolonged cooling may offset any potential benefit. Total liquid ventilation (TLV) provides both ultrafast cooling and rewarming. In previous reports, ultrafast cooling with TLV potently reduced neurological injury after experimental cardiac arrest in animals. We hypothesized that a brief period of rapid cooling and rewarming via TLV could also mitigate multiorgan failure (MOF) after ischemia-reperfusion induced by aortic cross-clamping.
METHODS: Anesthetized rabbits were submitted to 30 minutes of supraceliac aortic cross-clamping followed by 300 minutes of reperfusion. They were allocated either to a normothermic procedure with conventional ventilation (control group) or to hypothermic TLV (33°C) before, during, and after cross-clamping (pre-clamp, per-clamp, and post-clamp groups, respectively). In all TLV groups, hypothermia was maintained for 75 minutes and switched to a rewarming mode before resumption to conventional mechanical ventilation. End points included cardiovascular, renal, liver, and inflammatory parameters measured 300 minutes after reperfusion.
RESULTS: In the normothermic (control) group, ischemia-reperfusion injury produced evidence of MOF including severe vasoplegia, low cardiac output, acute kidney injury, and liver failure. In the TLV group, we observed gradual improvements in cardiac output in post-clamp, per-clamp, and pre-clamp groups versus control (53 ± 8, 64 ± 12, and 90 ± 24 vs 36 ± 23 mL/min/kg after 300 minutes of reperfusion, respectively). Liver biomarker levels were also lower in pre-clamp and per-clamp groups versus control. However, acute kidney injury was prevented in pre-clamp, and to a limited extent in per-clamp groups, but not in the post-clamp group. For instance, creatinine clearance was 4.8 ± 3.1 and 0.5 ± 0.6 mL/kg/min at the end of the follow-up in pre-clamp versus control animals (P = .0004). Histological examinations of the heart, kidney, liver, and jejunum in TLV and control groups also demonstrated reduced injury with TLV.
CONCLUSIONS: A brief period of ultrafast cooling with TLV followed by rapid rewarming attenuated biochemical and histological markers of MOF after aortic cross-clamping. Cardiovascular and liver dysfunctions were limited by a brief period of hypothermic TLV, even when started after reperfusion. Conversely, acute kidney injury was limited only when hypothermia was started before reperfusion. Further work is needed to determine the clinical significance of our results and to identify the optimal duration and timing of TLV-induced hypothermia for end-organ protection in hypoperfusion states.

鞘內注射氫嗎啡酮和嗎啡的剖宮產術後鎮痛：使用順序分配偏倚錢幣法確定 ED90

Intrathecal Hydromorphone and Morphine for Postcesarean Delivery Analgesia: Determination of the ED90 Using a Sequential Allocation Biased-Coin Method

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背景：鞘內注射（IT）嗎啡被認為是腰麻下剖宮產後的“金標準”鎮痛，最常用

的劑量在 100 至 200 μg。鞘內注射氫嗎啡酮用於剖宮產術後鎮痛經驗不足，最佳鎮痛劑量相關的研究資訊有限。此項研究目的為確定對擇期剖宮產後接受 IT 氫嗎啡酮鎮痛 90%患者對應的有效鎮痛劑量（ED90）和其與 IT 嗎啡的效價比。

方法：在這個劑量探索試驗中，80 名患者接受脊髓麻醉的剖腹產。參與者被隨機分配接受 IT 嗎啡或 IT 氫嗎啡，使用帶有偏置硬幣設計上下順序分配的方法確定的劑量以確定 ED90。所有患者除了 IT 阿片類藥物接受規範的多模式術後鎮痛。有效劑量定義為脊髓注射後 12 小時的對疼痛的數位回應得分≤3（比例 0-10）。

結果：IT 氫嗎啡酮、IT 嗎啡 ED90 分別是 75μg（95％可信區間[CI]，46-93μg）和 150μg（95％CI，145-185μg）。在這些劑量下，氫嗎啡酮、嗎啡有效鎮痛百分比（數位評定量表≤3）的 95％CI 分別是 64％至 100％、68％至 100％。探索性實驗結果表明，IT 嗎啡酮或 IT 嗎啡在常用劑量下噁心和瘙癢的發生率相似（分別為：P= 0.44 和 P =0.74；P= 0.67 和 P =0.38）。當使用 ED90 或更高劑量的 IT 阿片類藥物時， IT 氫嗎啡酮和 IT 嗎啡患者的鎮痛滿意率分別為 100％（21/21）和 95％（37/39）。

結論：IT 嗎啡對 IT 氫嗎啡酮產生剖宮產術後有效鎮痛比為 2：1。患者對兩者的滿意度都較高。

(董璐 譯 陳傑 校)

BACKGROUND: Intrathecal (IT) morphine is considered the "gold standard" for analgesia after cesarean delivery under spinal anesthesia, most commonly administered at a dose of 100 to 200 μg. There is less experience with IT hydromorphone for postcesarean analgesia and limited information on its optimal analgesic dose. We conducted this study to determine the effective analgesic dose for 90% patients (ED90) of IT hydromorphone that provides effective analgesia for women undergoing elective cesarean delivery and its potency ratio to IT morphine.

METHODS: In this dose-finding trial, 80 patients received spinal anesthesia for cesarean delivery. Participants were randomized to receive IT morphine or IT hydromorphone at a dose determined using up-down sequential allocation with a biased-coin design to determine ED90. All patients received standardized multimodal analgesia postoperatively in addition to IT opioid. An effective dose was defined as a numeric response score for pain of ≤3 (scale 0-10) 12 hours after spinal injection.

RESULTS: The ED90 was 75 μg (95% confidence interval [CI], 46-93 μg) for IT hydromorphone and 150 μg (95% CI, 145-185 μg) for IT morphine. At these doses, the 95% CI for the percentage of patients with effective analgesia (numeric rating scale ≤3) was 64% to 100% for hydromorphone and 68% to 100% for morphine. Exploratory findings showed that the incidence of nausea and pruritus was not different among the most commonly used doses of IT hydromorphone (P = 0.44 and P = 0.74) or IT morphine (P = 0.67 and P = 0.38, respectively). When administering IT opioids at ED90 doses or higher, 100% (21/21) of IT hydromorphone and 95% (37/39) of IT morphine patients were satisfied with their analgesia.

CONCLUSIONS: The ratio of IT morphine to IT hydromorphone for effective postcesarean analgesia is 2:1. Patient satisfaction was high with both medications.

先天性心臟病兒童圍術期右美托咪定的應用：一項來自 CCAS 和 STS 的先心病資料分析

The Perioperative Use of Dexmedetomidine in Pediatric Patients with Congenital

Heart Disease: An Analysis from the Congenital Cardiac Anesthesia Society-Society of Thoracic Surgeons Congenital Heart Disease Database

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背景：右美托咪定是一種選擇性 α-2 受體激動劑，其鎮靜作用及心肺影響特點使該藥在先心（CHD）兒童手術麻醉的應用方面有很大的吸引力。然而只有一些小的單中心研究提示右美在兒童先心患者圍術期的應用上越來受歡迎，但缺乏多中心的資料，並且對於不同年齡範圍、手術難度和醫療中心情況下如何調整用藥還並不清楚。本研究旨在分析患者疾病因素和中心水準對先心兒童圍術期應用右美托咪定的影響。

方法：為了研究 CHD 患者手術中右美托咪定的應用，本研究分析了 2010-2013 年 CCAS-STS 資料庫中所有關於體外迴圈手術的資料。比較圍術期右美托咪定應用與未應用患者的病情和手術特徵的差異。也對右美托咪定應用相關的選擇性預後進行描述。

結果：在 12142 項手術中，有 3600（29.6%）項圍術期用了右美托咪定（DEX），8542 個未應用（NoDEX）。兩組患者臨床特點不同：右美托咪定組患者病情較輕，手術風險較小。應用右美托咪定患者與未應用患者相比有更低的 STS 死亡率。與其總的低風險特徵相一致。且右美托咪定應用者較未應用者相比，有更好的預後。

結論：研究發現在兒童先心手術的麻醉中右美托咪定使用越來越多，尤其傾向於行非複雜性先心手術的大齡兒童。本研究所納入資料量在對於 CHD 患者的單一麻醉藥研究領域中首屈一指；也是首次同時對 CCAS 和 STS 先心疾病資料庫的麻醉資料進行分析。

(戴依利　譯　陳傑　校)

BACKGROUND: Dexmedetomidine is a selective α-2 receptor agonist with a sedative and cardiopulmonary profile that makes it an attractive anesthetic for pediatric patients with congenital heart disease (CHD). Although several smaller, single-center studies suggest thatdexmedetomidine use is gaining traction in the perioperative setting in children with CHD, there are limited multicenter data, with little understanding of the variation in use across age ranges, procedural complexity, and centers. The aim of this study was to use the CongenitalCardiac Anesthesia Society-Society of Thoracic Surgeons (CCAS-STS) registry to describe patient- and center-level variability in the use of dexmedetomidine in the perioperative setting in children with heart disease.

METHODS: To describe the use of dexmedetomidine in patients for CHD surgery, we analyzed all index cardiopulmonary bypass operations entered in the CCAS-STS database from 2010 to 2013. Patient and operative characteristics were compared between those who received intraoperative dexmedetomidine and those who did not. Selective outcomes associated with dexmedetomidine use were also described.

RESULTS: Of the 12,142 operations studied, 3600 (29.6%) received perioperative dexmedetomidine (DEX) and 8542 did not receive the drug (NoDEX). Patient characteristics were different between the 2 groups with the DEX group generally exhibiting both lower patient and procedural risk factors. Patients who received dexmedetomidine were more likely to have a lower level of Society of Thoracic Surgeons mortality complexity than patient who did not

receive it. Consistent with their overall lower risk profile, children in the DEX group also demonstrated improved outcomes compared with patients who did not receive dexmedetomidine.
CONCLUSIONS: We described the growing use of dexmedetomidine in children anesthetized for surgical repair of CHD. Dexmedetomidineappears to be preferentially given to older and larger children who are undergoing less complex CHD surgery. We believe that the data provided in this study are the largest investigating the use of an anesthetic drug in CHD patients. It is also the first analysis of the anesthesia data in the CCAS-STS Congenital Heart Disease database.

肌間溝神經阻滯在全肩關節置換術中的應用模式
The Patterns of Utilization of Interscalene Nerve Blocks for Total Shoulder Arthroplasty

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Anesthesia & Analgesia: 2016 123 758–761

肌間溝阻滯 (interscalene block, ISB)是全肩關節置換術(total shoulder arthroplasty, TSA)中全身麻醉的一項輔助方法。本研究目的提供目前國內實施肌間溝阻滯的全肩關節置換術病人的相關統計資料。對全國麻醉臨床效果註冊中心 2010 年至 2015 年的資料進行了回顧性分析。在 28810 例病例中，42.1%的病人接受一次肌間溝阻滯。只有 0.83%將區域神經阻滯作為主要的麻醉方式。2010 年至 2014 年之間，肌間溝阻滯在外科手術中的利用率有所增加(OR 比值，1.21；95%置信區間，1.19 -1.23；P < .0001)。此外報告了美國國內神經阻滯實施的人口分佈情況。明確了全肩關節置換術中區域神經阻滯的實施模式，為將來研究提供參考。
(傅丹雲　譯　陳傑　校)
The interscalene block (ISB) is a common adjunct to general anesthesia for total shoulder arthroplasty (TSA). The aim of the study was to report the current national demographics of the patients who are receiving ISB for TSAs. We performed a retrospective analysis of data from the National Anesthesia Clinical Outcomes Registry from 2010 to 2015. Of 28,810 cases, 42.1% received an ISB. Only 0.83% of cases received regional anesthesia as the primary anesthetic. From 2010 to 2014, there has been an increase in ISB utilization for this surgery (odds ratio, 1.21; 95% confidence interval, 1.19-1.23; P < .0001). Furthermore, we report a geographic distribution of block utilization in the United States. We have identified national patterns for the utilization of regional anesthesia for TSAs that may provide insight into future design of research studies.

先天性心臟病的心臟胚胎學和分子機制：麻醉醫生的引物
Cardiac Embryology and Molecular Mechanisms of Congenital Heart Disease: A Primer for Anesthesiologists

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Anesthesia & Analgesia: 2016 123 551–569

新生兒患有先天性心臟病的概率是在 0.4%到 5%，這對兒科麻醉醫生來說是特有的挑戰。此外,外科的進步提高了這些患者的生存率,並且有很多負責成人的麻醉醫師開始照顧一些曾經做過先天性心臟病手術的青年以及成年患者。在分

子和基因層面上瞭解關於異常心臟發育的知識擴展並增強了麻醉醫生對先天性心臟病的理解。在本文中,我們的目標是回顧當前有關的基因突變的知識以及與先天性心臟病的形成有關的細胞學的影響。鑒於目前先天性心臟病只能偶爾追溯到單個基因突變,我們高度重視研究人員在試圖確定心臟損傷的致病過程的具體步驟時所面臨的一些困難。
（董欣怡 譯 李士通 校）

Congenital heart disease is diagnosed in 0.4% to 5% of live births and presents unique challenges to the pediatric anesthesiologist. Furthermore, advances in surgical management have led to improved survival of those patients, and many adult anesthesiologists now frequently take care of adolescents and adults who have previously undergone surgery to correct or palliate congenital heart lesions. Knowledge of abnormal heart development on the molecular and genetic level extends and improves the anesthesiologist's understanding of congenital heart disease. In this article, we aim to review current knowledge pertaining to genetic alterations and their cellular effects that are involved in the formation of congenital heart defects. Given that congenital heart disease can currently only occasionally be traced to a single genetic mutation, we highlight some of the difficulties that researchers face when trying to identify specific steps in the pathogenetic development of heart lesions.

術中氧儲備指數與動脈血氧分壓的關係

The Relationship Between Oxygen Reserve Index and Arterial Partial Pressure of Oxygen During Surgery

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背景：在術中應用脈搏血氧飽和度（SpO_2）監測使我們能更及時地發現缺氧，因此減少了圍術期缺氧事件的發生。然而當動脈血氧分壓（PaO_2）低至70mmHg時可能脈搏血氧飽和度仍然顯示98%。因此，除非動脈血氧分壓接近這一水準，否則脈搏血氧飽和度並不能更及時地對動脈血氧含量進行預警。多波長脈衝氧飽和度能提供一個氧合指數的預測值，該預測值可能可以填補脈搏血氧飽和度 SpO_2>98%以上這段資料資訊。本研究評估了在術中多波長脈衝氧飽和度（ORI）與動脈血氧分壓（PaO_2）之間的關係。

方法：本試驗的研究物件為進行了動脈置管擬行術中動脈血氣分析的擇期手術患者。每名患者術中均持續進行多波長脈衝氧飽和度監測，監測資料存儲於試驗專用電腦中。應用回歸分析對ORI值與每次動脈血氣分析時的 PaO_2 值進行比較，並且通過連續的測量對二者的變化趨勢進行比較。通過對術中不同時間點重複測量受試者 PaO_2 和ORI，應用重複測量的線性混合效應回歸模型描述二者相互關係。應用 PaO_2 值為100和150mmHg時對應的ORI值對回歸曲線進行檢驗。應用特定主題隨機攔截的混合效應模型對ORI值與 PaO_2 進行比較。

結果：本研究收集了106名患者術中的ORI值和 PaO_2 測量值。回歸分析顯示ORI與 PaO_2 的相關性在 PaO_2 小於240mmHg這一區間內（r^2=0.536）要強於PaO2大於240mmHg這一區間（r^2=0.0016）。當 PaO_2 測量值≥100mmHg時所有樣本的ORI值均大於0.24。當 PaO_2 測量值≥150mmHg時96.6%的樣本的ORI值均大於0.55。重複測量的隨機攔截方差分量線性混合效應模型分析表明 PaO_2 與ORI顯著相關（β[95%可信區間]=0.002[0.0019-0.0022]；P<0.0001）。相似性

分析表明 PaO_2 的變化趨勢與 ORI 的變化趨勢顯著相關（β[95%可信區間]=0.0044[0.0040-0.0048]；P<0.0001）。

結論：這些研究結果提示當 SpO_2 在 98%以上時，ORI>0.24 可以作為識別 PaO_2≥100mmHg 的標誌。同理 ORI>0.55 也可以作為 PaO_2≥150mmHg 的臨界點。這些數值的實用性還需要進一步的研究進行評估。當 SpO_2>98%時，ORI 值下降至 0.24 附近可能進一步提示 PaO_2 已經跌至 100mmHg 附近。ORI 對臨床干預的實用性是建立在持續監測的基礎上的，需要進一步研究支援。

（陳峰 譯 李士通 校）

BACKGROUND: The use of intraoperative pulse oximetry (SpO_2) enhances hypoxia detection and is associated with fewer perioperative hypoxic events. However, SpO2 may be reported as 98% when arterial partial pressure of oxygen (PaO_2) is as low as 70 mm Hg. Therefore, SpO_2 may not provide advance warning of falling arterial oxygenation until PaO_2 approaches this level. Multiwave pulse co-oximetry can provide a calculatedoxygen reserve index (ORI) that may add to information from pulse oximetry when SpO_2 is >98%. This study evaluates the ORI to PaO_2 relationship during surgery.

METHODS: We studied patients undergoing scheduled surgery in which arterial catheterization and intraoperative arterial blood gas analysis were planned. Data from multiple pulse co-oximetry sensors on each patient were continuously collected and stored on a research computer. Regression analysis was used to compare ORI with PaO_2 obtained from each arterial blood gas measurement and changes in ORI with changes in PaO_2 from sequential measurements. Linear mixed-effects regression models for repeated measures were then used to account for within-subject correlation across the repeatedly measured PaO_2 and ORI and for the unequal time intervals of PaO_2 determination over elapsed surgical time. Regression plots were inspected for ORI values corresponding to PaO_2 of 100 and 150 mm Hg. ORI and PaO_2 were compared using mixed-effects models with a subject-specific random intercept.

RESULTS: ORI values and PaO_2 measurements were obtained from intraoperative data collected from 106 patients. Regression analysis showed that the ORI to PaO_2 relationship was stronger for PaO2 to 240 mm Hg (r = 0.536) than for PaO_2 over 240 mm Hg (r = 0.0016). Measured PaO_2 was ≥100 mm Hg for all ORI over 0.24. Measured PaO_2 was ≥150 mm Hg in 96.6% of samples when ORI was over 0.55. A random intercept variance component linear mixed-effects model for repeated measures indicated that PaO_2 was significantly related to ORI (β[95% confidence interval] = 0.002 [0.0019-0.0022]; P < 0.0001). A similar analysis indicated a significant relationship between change in PaO_2 and change in ORI (β [95% confidence interval] = 0.0044 [0.0040-0.0048]; P < 0.0001).

CONCLUSIONS: These findings suggest that ORI >0.24 can distinguish PaO_2 ≥100 mm Hg when SpO2 is over 98%. Similarly, ORI > 0.55 appears to be a threshold to distinguish PaO_2 ≥150 mm Hg. The usefulness of these values should be evaluated prospectively. Decreases in ORI to near 0.24 may provide advance indication of falling PaO_2 approaching 100 mm Hg when SpO2 is >98%. The clinical utility of interventions based on continuous ORI monitoring should be studied prospectively.

精氨酸酶抑制劑在轉基因鐮狀細胞小鼠模型中可逆轉血管內皮功能障礙，肺動脈高壓和血管硬化

Arginase Inhibition Reverses Endothelial Dysfunction, Pulmonary Hypertension, and Vascular Stiffness in Transgenic Sickle Cell Mice

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背景：鐮狀細胞病（SCD）所致的溶血可引起精氨酸酶的釋放和啟動，而精氨酸酶則可與一氧化氮（NO）的合成與產生互相調節。然而，單純補充兩者的共同底物 L-精氨酸並不能提高 NO 的生物利用度。在本次研究中，我們對於精氨酸酶抑制劑可提高 NO 的生物利用度，從而降低 SCD 轉基因小鼠的全身和肺血管內皮功能障礙這一假設進行了驗證。
方法：本次研究中，我們選擇 5 個月大的轉基因鐮狀細胞小鼠作為實驗組（SC 組），而與其年齡匹配的野生型作為對照組（WT 組）。其中，SC 組小鼠又分為經精氨酸酶抑制劑處理組（即使用 2(S)氨基-6-溴己酸（ABH），約 400μg/日，處理 4 周）和未經精氨酸酶抑制劑處理組。
結果：未接受精氨酸酶抑制劑處理的 SC 組小鼠，其血管精氨酸酶活性顯著高於 WT 組（SC 未處理組：346±69.3 pmol 尿素/mg 蛋白/分鐘，WT 組 69±17.3 pmol 尿素/mg 蛋白/分鐘；P = 0.0043；n = 4–5（每組動物數））。使用 ABH 治療可顯著降低精氨酸酶活性，使其接近于 WT 組水準（SC + ABH 組：125.2±17.3 pmol 尿素/mg 蛋白/分鐘；P = 0.0213）。與 WT 組相比，SC 未處理組小鼠的主動脈中 NO 顯著減少，活性氧（ROS）生成顯著增加（SC 未處理組 NO 螢光率 0.76±0.14 RFU/s，WT 組 NO 螢光率 1.34±0.17 RFU/s；P = 0.0005；SC 未處理組 ROS 螢光率：3.96±1.70 RFU/s，WT 組 ROS 螢光率 1.63±1.20 RFU/s，P = 0.0039；n = 3（每組動物數））。接受 ABH 處理 4 周的 SC 組小鼠，其 NO 水準（螢光率：1.16±0.16 RFU/s）和活性氧水準（螢光率：2.02±0.45 RFU/s）與年齡匹配的 WT 組基本持平（n = 3 （每組動物數））。SC 組小鼠主動脈對於乙醯膽鹼的內皮依賴性血管舒張反應顯著弱於 WT 組小鼠（SC 組：57.7%±8.4% ，WT 組：80.3%±11%；P = 0.02；n = 6（每組動物數））。組間比較內皮依賴性反應無顯著差異。SC 組小鼠右室輸出指數和收縮末期彈性無顯著差異（4.60±0.51 vs 2.9±0.85 ml/min/ 100 g 和 0.89±0.48 vs 0.58±0.11 mmHg/μL），但 SC 組小鼠肺血管阻力和右心室收縮末期壓力更大（2.9±0.28 vs 5.5±2.0 mmHg×min/μL / 100 g 和 18.9±1.1 vs 23.1±4 mmHg；N =8（每組動物數））。SC 組小鼠的脈搏速度（用於測量動脈僵硬度）顯著高於 WT 組（3.74±0.54 vs 3.25±0.21m/s；N = 20（每組動物數）），經精氨酸酶抑制劑處理 4 周可顯著降低 SC 組小鼠的血管硬化，使其與 WT 組接近（P = 0.0009）。
結論：精氨酸酶抑制劑可提高 NO 的生物利用度，進而減少 SCD 轉基因小鼠的全身和肺血管內皮功能障礙。因此，精氨酸酶是 SCD 心血管功能障礙的一個潛在治療靶點。
（陸曉斐 譯 李士通 校）
BACKGROUND: In sickle cell disease (SCD), hemolysis results in the release and activation of arginase, an enzyme that reciprocally regulates nitric oxide (NO) synthase activity and thus, NO production. Simply supplementing the common substrate L-arginine, however, fails to improve NO bioavailability. In this study, we tested the hypothesis that arginase inhibition would improve NO bioavailability and thereby attenuate systemic and pulmonary vascular endothelial dysfunction in transgenic mice with SCD.
METHODS: We studied 5-month-old transgenic sickle cell (SC) mice and age

matched wild-type (WT) controls. SC mice were treated with the arginase inhibitor, 2(S)-amino-6-boronohexanoic acid (ABH; approximately 400 μg/d) for 4 weeks or left untreated.
RESULTS: Vascular arginase activity was significantly higher at baseline in untreated SC mice compared to WT controls (SC versus WT, 346 ± 69.3 vs 69 ± 17.3 pmol urea/mg protein/minute; P = 0.0043; n = 4–5 animals per group). Treatment with ABH may significantly decrease arginase activity to levels near WT controls (SC + ABH 125.2 ± 17.3 pmol urea/mg protein/minute; P = 0.0213). Aortic strips from untreated SC mice showed decreased NO and increased reactive oxygen species (ROS) production (NO: fluorescence rate 0.76 ± 0.14 vs 1.34 ± 0.17 RFU/s; P = 0.0005 and ROS: fluorescence rate 3.96 ± 1.70 vs 1.63 ± 1.20 RFU/s, P = 0.0039; n = 3– animals per group). SC animals treated with ABH for 4 weeks demonstrated NO (fluorescence rate: 1.16 ± 0.16) and ROS (fluorescence rate: 2.02 ± 0.45) levels comparable with age-matched WT controls (n = 3– animals per group). The maximal endothelial-dependent vasorelaxation response to acetylcholine was impaired in aortic rings from SC mice compared with WT (57.7% ± 8.4% vs 80.3% ± 11.0%; P = 0.02; n = 6 animals per group). The endothelial-independent response was not different between groups. In SC mice, the right ventricular cardiac output index and end-systolic elastance were similar (4.60 ± 0.51 vs 2.9 ± 0.85 mL/min/100 g and 0.89 ± 0.48 vs 0.58 ± 0.11 mm Hg/μL), whereas the pulmonary vascular resistance index and right ventricular end-systolic pressure were greater (2.9 ± 0.28 vs 5.5 ± 2.0 mm Hg × min/μL/100 g and 18.9 ± 1.1 vs 23.1 ± 4.0 mm Hg; n = 8 animals per group). Pulse wave velocity (a measure of arterial stiffness) was greater in SC mice compared with WT (3.74 ± 0.54 vs 3.25 ± 0.21 m/s; n = 20 animals per group), arginase inhibition for 4 weeks significantly reduced the vascular SC phenotype to one similar to WT animals (P = 0.0009).
CONCLUSIONS: Arginase inhibition improves NO bioavailability and thereby attenuates systemic and pulmonary vascular endothelial dysfunction in transgenic mice with SCD. Therefore, arginase is a potential therapeutic target in the treatment of cardiovascular dysfunction in SCD.

在腰硬聯合阻滯分娩鎮痛中行硬膜外容量擴充不會升高感覺阻滯平面

Epidural Volume Extension During Combined Spinal-Epidural Labor Analgesia Does Not Increase Sensory Block

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背景：腰硬聯合麻醉（CSE）廣泛用於分娩鎮痛。硬膜外容量擴充（EVE）是在硬膜外腔注入溶液壓迫硬脊膜，促使腦脊液向頭端擴散。我們假設，在 CSE 中用　生理鹽水作 EVE，15 分鐘後感覺阻滯平面升高。我們預計 CSE 中行 EVE 比未行 EVE（NEVE）的疼痛評分降低，減少鎮痛起效時間、運動阻滯。
方法：我們隨機分配 60 例子宮頸口擴張小於 5 釐米的足月分娩產婦行 CSE 在導管置入前通過 TUOHY 針注入 10 mL 生理鹽水或行 CSE NEVE。鞘內注射鎮痛由 2 mg 純布比卡因和 10 芬太尼（總量 1 mL）組成。應用盲法由研究人員評估感覺阻滯平面、痛覺阻滯平面和 30 分鐘運動阻滯。主要測量指標是 15 分鐘最高感覺阻滯平面的中位數。

結果：對 54 名產婦進行了分析。15 分鐘（平均差，1 節段；95%置信區間的中位數差異，0 到 2；P = 0.22）和 30 分鐘（平均差，0 節段；95%置信區間，2 到 2；P = 0.76）最高感覺阻滯平面的中位數無顯著差異。在最高感覺阻滯平面、最低疼痛評分和最快鎮痛起效時間的組間比較無顯著差異。
結論：我們發現感覺阻滯平面和疼痛分數在 EVE 和 NEVE 組間無顯著差異。我們的研究表明，在對產婦應用 CSE 分娩鎮痛中加行 EVE 並沒有優化鎮痛技術。（周延青 譯 李士通 校 ）

BACKGROUND: Combined spinal-epidural (CSE) analgesia is widely used for delivering labor analgesia. Epidural volume extension (EVE) involves the injection of fluid into the epidural space compressing the dural sac, causing cephalad shift of the cerebral spinal fluid. Our hypothesis was that EVE with 10 mL normal saline during CSE would increase the sensory block height at 15 minutes after intrathecal injection. We expected EVE to decrease pain scores, decrease analgesia onset time, and decrease motor block compared with performing CSE without EVE (NEVE).
METHODS: We randomly assigned 60 healthy term laboring nulliparous parturients with cervical dilation <5 cm to receive CSE either with EVE of 10 mL normal saline through the Tuohy needle before catheter insertion or CSE NEVE. Intrathecal analgesia consisted of 2 mg plain bupivacaine and 10 μg fentanyl (1 mL total). A blinded researcher assessed sensory dermatome level, analgesia, and motor blockade at regular intervals for 30 minutes. The primary outcome measure was the median peak sensory dermatome level at 15 minutes.
RESULTS: Fifty-four parturients were analyzed. There was no significant difference in peak sensory dermatome levels at 15 minutes (median difference, 1 dermatome level; 95% confidence interval of median difference, 0 to 2; P = 0.22) and 30 minutes (median difference, 0 dermatome level; 95% confidence interval, -2 to 2; P = 0.76). There was no difference in the time to peak dermatome, minimum pain score, or the time to minimum pain score between groups.
CONCLUSIONS: We found no significant difference between groups with regard to sensory dermatome level or pain scores when using EVE compared with NEVE. Our study demonstrates that addition of EVE does not offer superior analgesia when using a CSE technique for parturients requesting labor analgesia.

靜脈內篩檢程式在兒科患者低流量輸液泵給藥中的使用

Syringe Pump Performance Maintained with IV Filter Use During Low Flow Rate Delivery for Pediatric Patients

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背景：複雜外科手術和危重患兒靜脈藥物的精確輸注依賴注射器輸液泵。低流量和內置篩檢程式的使用可能影響藥物輸注。為了評價內置篩檢程式在消除低流量注射器輸液泵使用時的空氣和/或污染物的效果，我們比較了在設定流量下使用和不使用內置篩檢程式時的實際測得流量。
方法：分別使用和不使用篩檢程式製作靜脈輸注設備（篩檢程式組和對照組）連接到一個 10ml 注射器，再裝上一個輸液泵，連接到 16cm 的單腔導管。導管懸浮在生理鹽水液柱中用來模擬中心靜脈迴圈的壓力。採用重量法在預定的時間間隔測量注射量和計算流量。實驗設定對照組和篩檢程式組依次採用 1、0.8、0.6 和 0.4ml/h 的初始流量進行。在每一個試驗中，流量改為雙倍初始流

量，然後再回到初始流量，用於分析給藥過程中通常要求的反應輸注泵性能的滴定率。這些條件（初始流量、雙倍初始流量、回到初始流量）分別進行了獨立的穩態流量和到達穩定狀態的時間分析，而他們的平均值用來進行百分偏差分析。對照組和篩檢程式組之間的差異採用 t 檢驗與多樣性調整（使用 n = 3 重複每組）。

結果：兩組從 0 到初始流量（啟動延遲）的平均時間均小於 1 分鐘差異無統計學意義（P = 1.0）。兩組在任意流量或任意階段（初始流量、雙倍初始流量、回到初始流量），開始輸注和流量改變時達到穩態流量的平均時間沒有統計學差異（範圍 0.8-5.5 分鐘），儘管實驗不足以發現微小的時間差異。總的來說，每個實驗的平均穩態流量低於設定的流量，為負的平均百分偏差。在 1.0ml/h 初始流量試驗中，篩檢程式組較對照組初始流量獲得穩態流量低（P = 0.04），雙倍初始流量獲得穩態流量低（P = 0.04），回到初始流量獲得穩態流量也低（P = 0.06），雖然與對照組相比，在 0.8ml/h 、0.6ml/h 或其他組實驗中沒有觀察到相同結果。

結論：隨著低流量輸液泵在複雜外科和兒科危重病人中的應用，使用內置篩檢程式並不能顯著改善輸液泵給藥過程中的啟動延遲，流量變化，和達到穩態流量的時間。不論是否使用篩檢程式，整體流量均低於設定流量。

（章健萍 譯 李士通 校）

BACKGROUND: Complex surgical and critically ill pediatric patients rely on syringe infusion pumps for precise delivery of IV medications. Low flow rates and in-line IV filter use may affect drug delivery. To determine the effects of an in-line filter to remove air and/or contaminants on syringe pump performance at low flow rates, we compared the measured rates with the programmed flow rates with and without in-line IV filters.

METHODS: Standardized IV infusion assemblies with and without IV filters (filter and control groups) attached to a 10-mL syringe were primed and then loaded onto a syringe pump and connected to a 16-gauge, 16-cm single-lumen catheter. The catheter was suspended in a normal saline fluid column to simulate the back pressure from central venous circulation. The delivered infusate was measured by gravimetric methods at predetermined time intervals, and flow rate was calculated. Experimental trials for initial programmed rates of 1.0, 0.8, 0.6, and 0.4 mL/h were performed in control and filter groups. For each trial, the flow rate was changed to double the initial flow rate and was then returned to the initial flow rate to analyze pump performance for titration of rates often required during medication administration. These conditions (initial rate, doubling of initial rate, and return to initial rate) were analyzed separately for steady-state flow rate and time to steady state, whereas their average was used for percent deviation analysis. Differences between control and filter groups were assessed using Student t tests with adjustment for multiplicity (using n = 3 replications per group).

RESULTS: Mean time from 0 to initial flow (startup delay) was <1 minute in both groups with no statistical difference between groups (P = 1.0). The average time to reach steady-state flow after infusion startup or rate changes was not statistically different between the groups (range, 0.8-5.5 minutes), for any flow rate or part of the trial (initial rate, doubling of initial rate, and return to initial rate), although the study was underpowered to detect small time differences. Overall, the mean steady-state flow rate for each trial was below the programmed flow rate with negative mean percent deviations for each trial. In the 1.0-mL/h initial rate trial, the steady-state flow rate attained was lower in the filter than the control group for the initial rate (P = 0.04)

and doubling of initial rate (P = 0.04) with a trend during the return to initial rate (P = 0.06), although this same effect was not observed when doubling the initial rate trials of 0.8 or 0.6 mL/h or any other rate trials compared with the control group.
CONCLUSIONS: With low flow rates used in complex surgical and pediatric critically ill patients, the addition of IV filters did not confer statistically significant changes in startup delay, flow variability, or time to reach steady-state flow of medications administered by syringe infusion pumps. The overall flow rate was lower than programmed flow rate with or without a filter.

可樂定不降低非心臟手術後的疼痛或阿片類藥物的用量

Clonidine Does Not Reduce Pain or Opioid Consumption After Noncardiac Surgery

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背景：可樂定是一種具有鎮痛作用的 α2 腎上腺素受體激動劑。然而，圍手術期可樂定的鎮痛效果尚不清楚。因此，我們驗證了非心臟手術後的最初 72 小時內可樂定降低了疼痛評分和阿片類藥物累積用量這一假說。
方法：624 例全身麻醉和脊髓麻醉的擇期非心臟手術的病人被納入圍術期缺血評估-2 試驗的子研究中。術前 2-4 小時將患者隨機分組，分別為口服可樂定 0.2mg 組或口服安慰劑組，接著給予 0.2mg/天透皮可樂定貼片或安慰劑，並維持至術後 72 小時，再對術後 72 小時疼痛評分和阿片類藥物的用量進行了評估。
結果：與安慰劑相比，可樂定在減少阿片類藥物用量上沒有作用，估計均值比為 0.98（95%置信區間，0.70-1.38）；P = 0.92。可樂定組阿片類藥物用量的中位數（Q1、Q3）為 63（30，154）mg 嗎啡當量，這與安慰劑組 60（30，128）mg 嗎啡當量相似。此外，用 11 點量表評估疼痛評分，發現對兩組的疼痛評分無明顯影響，估計平均差值為 0.12（95%置信區間，-0.02 -0.26）；P = 0.10。可樂定組的患者平均疼痛評分為 3.6±1.8，安慰劑組患者平均疼痛評分 3.6±1.8。
結論：可樂定不降低患者非心臟手術恢復過程中阿片類藥物的用量或疼痛評分。
（呂良策 譯 李士通 校）

BACKGROUND: Clonidine is an α2-adrenoceptor agonist, which has analgesic properties. However, the analgesic efficacy of perioperative clonidine remains unclear. We, therefore, tested the hypothesis that clonidine reduces both pain scores and cumulative opioid consumption during the initial 72 hours after noncardiac surgery.
METHODS: Six hundred twenty-four patients undergoing elective noncardiac surgery under general and spinal anesthesia were included in this substudy of the PeriOperative ISchemia Evaluation-2 trial. Patients were randomly assigned to 0.2 mg oral clonidine or placebo 2 to 4 hours before surgery, followed by 0.2 mg/d transdermal clonidine patch or placebo patch, which was maintained until 72 hours after surgery. Postoperative pain scores and opioid consumption were assessed for 72 hours after surgery.

RESULTS: Clonidine had no effect on opioid consumption compared with placebo, with an estimated ratio of means of 0.98 (95% confidence interval, 0.70-1.38); P = 0.92. Median (Q1, Q3) opioid consumption was 63 (30, 154) mg morphine equivalents in the clonidine group, which was similar to 60 (30, 128) mg morphine equivalents in the placebo group. Furthermore, there was no significant effect on pain scores, with an estimated difference in means of 0.12 (95% confidence interval, -0.02 to 0.26); 11-point scale; P = 0.10. Mean pain scores per patient were 3.6 ± 1.8 for clonidine patients and 3.6 ± 1.8 for placebo patients.
CONCLUSIONS: Clonidine does not reduce opioid consumption or pain scores in patients recovering from noncardiac surgery.

在瑞芬太尼誘發的痛覺超敏中，PICK1 調節氨甲基膦酸(AMPA)受體的表達和轉運

PICK1 Regulates the Expression and Trafficking of AMPA Receptors in Remifentanil-Induced Hyperalgesia

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背景：瑞芬太尼因為比其他阿片類止痛藥誘導更快速，從而被廣泛應用於臨床麻醉，但其也更容易發生痛覺超敏。啟動的門冬氨酸受體（NMDA 受體）是誘發瑞芬太尼痛覺超敏的關鍵部分。和 NMDA 受體一樣，AMPARs（α-氨基-3-羥基-5-甲基-4-異唑丙酸受體），在突觸後膜是離子型興奮性谷氨酸受體，參與急性和慢性疼痛的傳遞。PICK1，C 激酶 1 蛋白相互作用蛋白，在 NMDA 受體介導的含 GluR2（谷氨酸受體 2）亞單位的 AMPARs 受體的內化中扮演一個重要的角色，並作用於炎症性疼痛的發生和持續。本研究的目的是，驗證 PICK1 能通過調節 AMPAR 在脊髓中的表達和轉運，從而在瑞芬太尼誘發的痛覺過敏中起作用這一假說。
方法：使用大鼠模型進行瑞芬太尼靜脈灌注來誘發痛覺過敏。我們首先測量瑞芬太尼灌注前 24 小時和注入後 2、6、24、48 小時的機械和熱痛覺過敏變化。在脊髓中 PICK1 的 mRNA 和蛋白質的表達、AMPAR 亞基的表達和轉運分別由反轉錄定量 PCR、免疫組化和免疫印跡測得。此外，我們通過鞘內注射 PICK1 反義寡去氧核苷酸來沉默 PICK1 的表達，研究 PICK1 缺乏對瑞芬太尼誘發的痛覺過敏和 AMPARs 表達和轉運的影響。
結果：在疼痛閾值中發現了一個明顯的時間-組別相關性(縮足反應的閾值和縮足反應的潛伏期；差異有統計學意義， P<.0001)。瑞芬太尼灌注在不同時間點引起不同的痛覺過敏 (P<.0001)，且部分因 PICK1 的沉默而逆轉 (P<.007)。此外，在脊髓背角神經元，瑞芬太尼的注入增加了 PICK1 的 mRNA 和蛋白的表達 (P<.0001)和細胞膜上谷氨酸 1、2 受體的內化 (P<.0011)。更重要的是，PICK1 缺乏可以在脊髓背角處減弱瑞芬太尼誘導的 GluR2 內化 (P<.01)，但不影響瑞芬太尼誘導的細胞膜上的 GluR1 表達(P≥.985)。
結論：這些結果表明，PICK1 缺乏可能會通過調節含 GluR2 亞單位的 AMPAR 在脊髓背角的表達和轉運從而逆轉瑞芬太尼誘發的痛覺過敏。
（俞泳 譯 李士通 校）

BACKGROUND: Remifentanil is used widely in clinical anesthesia because it induces more rapid and more common hyperalgesia than other opioid analgesics. Activation of N-methyl-D-aspartate (NMDA) receptors takes a pivotal part in remifentanil-induced hyperalgesia. Like NMDA receptors, the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs) are excitatory ion glutamate receptors in postsynaptic membrane, which are involved in the transmission of both acute and chronic pain. Protein interacting with C kinase 1 (PICK1) plays an important role in NMDA receptor-mediated internalization of glutamate receptor 2 (GluR2)-containing AMPARs and contributes to the induction and maintenance of inflammation-induced pain. This study aimed to test the hypothesis that PICK1 contributes to remifentanil-induced hyperalgesia by regulating AMPAR expression and trafficking in the spinal cord.
METHODS: Using a rat model of remifentanil-induced hyperalgesia by intravenous infusion of remifentanil, we first measured changes in mechanical and thermal hyperalgesia at 24 hours before remifentanil infusion and 2, 6, 24, and 48 hours after infusion. PICK1 mRNA and protein expression and AMPAR subunit expression and trafficking in the spinal cord were then detected by reverse transcription-qualitative polymerase chain reaction, immunohistochemistry, and Western blot. In addition, we knocked down PICK1 expression by intrathecal administration of PICK1 antisense oligodeoxynucleotide to investigate the effects of PICK1 deficiency on remifentanil-induced hyperalgesia and the expression and trafficking of AMPARs.
RESULTS: A significant time-group interaction was found for nociceptive thresholds (paw withdrawal threshold and paw withdrawal latency; all $P < .0001$). Remifentanil infusion induced distinct hyperalgesia at different time points ($P < .0001$), which was partly reversed by PICK1 knockdown ($P < .007$). Besides, remifentanil infusion increased the expression of PICK1 mRNA and protein ($P < .0001$) and the membrane GluR1 and GluR2 internalization in spinal dorsal horn neurons ($P < .0011$). More importantly, PICK1 deficiency could attenuate remifentanil-induced GluR2 internalization in the spinal cord dorsal horn ($P < .01$) but had no effect on remifentanil-induced membrane GluR1 expression ($P \geqslant .985$).
CONCLUSIONS: These results indicate that PICK1 deficiency might reverse remifentanil-induced hyperalgesia through regulating GluR2-containing AMPAR expression and trafficking in the spinal cord dorsal horn.